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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,277	09/10/2004	Hiroshi Kasai	SHIGA8.001APC	3845

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EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/507,277	KASAI, HIROSHI	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *7-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/10/04,4/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-6 in the reply filed on 4/10/2006 is acknowledged. Claims 7-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/10/2006.

Claim Objections

Claim 4 is objected to because of the following informalities: Claim 4 recites the notation 8-OH-dG twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites 8-hydroxygunosines and the term ribonucleosides within parentheses. Since the plural is recited for the said terms it is not clear if 8-hydroxyguanosines includes one or more of other substituted guanosines and ribonucleosides includes one of more of any ribonucleosides. The term ribonucleosides is recited within parentheses. It is not clear if this term is part of the claim limitation. It is not clear what applicants intend.

The term ribonucleosides is also recited within parentheses in claim 4.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Yanagawa et al (Nucleic Acid Symposium Series, 1991, 25, 113-114).

Yanagawa et al teach the purification of 8-hydroxyguanosine (oxidatively damaged guanine nucleoside) from a nucleoside mixture (sample) comprising a first purification step by anion-exchange chromatography (page 113, right column, Materials and Methods; limitation of instant claim 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa et al (Nucleic Acid Symposium Series, 1991, 25, 113-114).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 2 is drawn to a method of purification of oxidatively damaged guanine nucleosides wherein the guanine is 8-hydroxydeoxyguanosine.

Yanagawa et al teach the purification of 8-hydroxyguanosine (oxidatively damaged guanine nucleoside) from a nucleoside mixture (sample) comprising a first purification step by anion-exchange chromatography (page 113, right column, Materials and Methods). However, Yanagawa et al do not teach the purification of 8-hydroxydeoxyguanosine.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to purify 8-hydroxydeoxyguanosine by anion-exchange chromatography since the use of such a method using the structurally analogous 8-hydroxyguanosine is taught in the prior art.

One of ordinary skill in the art would be motivated to purify 8-hydroxydeoxyguanosine by the method as instantly claimed since such a purification gives a good recovery of the analogous 8-hydroxyguanosine. One of ordinary skill in the art would expect the recovery of pure 8-hydroxydexoyguanosine also to be similar to that of 8-hydroxyguanosine because of its structural similarity.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Carcinogenesis, 1989, 10(5), 827-832).

Claim 3 is drawn to a method of purification of 8-hydroxydeoxygunosines contained in a sample wherein 8-hydroxygunosines are previously added to the sample as an internal standard marker.

Park et al, drawn to detection of DNA adducts, teach that guanosine ribonucleosides elute immediately before the corresponding deoxyribonucleosides in high performance liquid chromatography (page 829, left column, 19-22 and Figure 2). From this teaching one of ordinary skill in the art will recognize that based on the position of the hydroxyguanosine in the HPLC chromatogram the peak due to the deoxyguanosine can be easily identified. In other words hydroxyguanosine can serve as a marker for the corresponding deoxyguanosine.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use 8-hydroxyguanosine as an internal standard marker in a sample containing the corresponding deoxygunosine in a method of purification of hydroxydeoxyguanosine since such a method is seen to be taught in the prior art.

One of ordinary skill in the art will be motivated to use the hydroxyguanosine as an internal standard marker since it provides a means for quick and easy identification of the hydroxydeoxyguanosine in the HPLC chromatogram.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa et al (Nucleic Acid Symposium Series, 1991, 25, 113-114) in combination with Park et al (Carcinogenesis, 1989, 10(5), 827-832).

Claim 4 is drawn to a purification method for 8-hydroxydeoxyguanosine contained in a sample wherein 8-hydroxyguanosine is previously added to the sample comprising first purification by anion-exchange chromatography followed by a second purification of the fraction containing the 8-hydroxydeoxyguanosine by reverse phase chromatography.

Yanagawa et al teach the purification of 8-hydroxyguanosine (oxidatively damaged guanine nucleoside) from a nucleoside mixture (sample) comprising a first purification step by anion-exchange chromatography (page 113, right column, Materials and Methods). However, Yanagawa et al do not teach the purification of 8-hydroxydeoxyguanosine contained in a sample wherein 8-hydroxyguanosine is previously added to the sample comprising first purification by anion-exchange chromatography followed by a second purification of the fraction containing the 8-hydroxydeoxyguanosine by reverse phase chromatography.

Park et al, drawn to detection of DNA adducts, teach that guanosine ribonucleosides elute immediately before the corresponding deoxyribonucleosides in high performance reverse phase liquid chromatography (page 829, left column, 19-22 and Figure 2, page 828, right column, see under HPLC-EC). From this teaching one of ordinary skill in the art will recognize that based on the position of the hydroxyguanosine in the HPLC chromatogram the peak due to the deoxyguanosine can be easily identified. In other words hydroxyguanosine can serve as a marker for the corresponding deoxyguanosine. It can also be seen form the teaching of Park that reverse phase chromatography gives good separation of deoxyguanosine.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to purify8-hydroxydeoxyguanosine contained in a sample wherein 8-

hydroxyguanosine is previously added to the sample as instantly claimed since the use of the two methods individually for purification of the compounds is seen to be taught in the prior art.

One of ordinary skill in the art will be motivated to use the method as instantly claimed because the presence of hydroxyguanosine in the sample containing the corresponding hydroxydeoxyguanosine serves as an internal standard marker and provides a means for quick and easy identification of the hydroxydeoxyguanosine in the HPLC chromatogram. Both chromatographic methods are seen to give good separation of the desired products and the use of both the chromatographic methods one after the other will give a highly pure product for quantization of oxidative damage.

Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa et al (Nucleic Acid Symposium Series, 1991, 25, 113-114) in combination with Park et al (Carcinogenesis, 1989, 10(5), 827-832) and Loft et al (Journal of Toxicology and Enivronmental Health 1993, 40, 391-404).

Claims 5-6 are drawn to a purification method for oxidatively damaged guanine nucleosides and in particular 8-hydroxydeoxyguanosines in a sample wherein the sample is urine.

Yanagawa et al teach the purification of 8-hydroxyguanosine (oxidatively damaged guanine nucleoside) from a nucleoside mixture (sample) comprising a first purification step by anion-exchange chromatography (page 113, right column, Materials and Methods). However, Yanagawa et al do not teach the purification of 8-hydroxydeoxyguanosine wherein the sample is urine.

Park et al, drawn to detection of DNA adducts, teach that guanosine ribonucleosides elute immediately before the corresponding deoxyribonucleosides in high performance reverse phase liquid chromatography (page 829, left column, 19-22 and Figure 2, page 828, right column, see under HPLC-EC). From this teaching one of ordinary skill in the art will recognize that based on the position of the hydroxyguanosine in the HPLC chromatogram the peak due to the deoxyguanosine can be easily identified. In other words hydroxyguanosine can serve as a marker for the corresponding deoxyguanosine. It can also be seen form the teaching of Park that reverse phase chromatography gives good separation of deoxyguanosine and Park also teaches that his method has a high degree of specificity and can be used for the quantization of damaged products not just in hydrolysates but also in urine.

Loft teaches the analysis and separation of 8-hydroxydeoxyguanosine in urine using HPLC (abstract and page 393, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to purify8-hydroxydeoxyguanosine contained in a sample of urine as instantly claimed since the use of the two chromatographic methods individually for purification of the said in compounds in a urine sample is seen to be taught in the prior art.

One of ordinary skill in the art will be motivated to use the method as instantly claimed because the presence of hydroxyguanosine in the sample containing the corresponding hydroxydeoxyguanosine serves as an internal standard marker and provides a means for quick and easy identification of the hydroxydeoxyguanosine in the HPLC chromatogram. Both chromatographic methods are seen to give good separation of the desired products from different

samples including urine and the use of both the chromatographic methods one after the other will give a highly pure product for quantization of oxidative damage.

Conclusion

Claims 1-6 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK

6/22/06

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